and in the final analysis are enforced by compulsion. Medicine's strengths on the other hand are more fragile and often quite intangible. They rest upon the skill, motivation and unique competence of the health professional, are directed to the needs of the individual who is or may become a patient, and derive their public support from good performance which is understood and appreciated.

The medical profession has yet to perfect the skills needed to bring these less tangible strengths of medicine fully to bear upon the decision processes in the social, economic and political aspects of government involvement in health care. The Fourth Progress Report of the Committee on the Role of Medicine in Society (1968)[3] concerned itself in part with how this might be approached. It noted that it is public opinion which finally decides all the important public issues, whether in medicine or in government. It further noted that so far this fact has been better understood by government than it has by medicine. Medicine needs to develop a new and vastly improved technology for its advocacy of quality, quantity and efficiency in health care, if it is to gain the full understanding and active support of public opinion. There have been some beginnings and some accomplishments. But much more is needed. New and expanded social tactics of communication and involvement should be developed and used. New and more effective tactics to bring economic pressures to bear in various situations may soon be needed, and studies of how this might be done should be begun immediately. And much more sophisticated political tactics with far greater emphasis on involvement with others of like purposes and with much more effective use made of medicine's knowledge and expertise in patient care are necessary. These kinds of skills should be developed soon and put to use in the interest of both the patient and an all too often uninformed or misinformed public. It is already getting late.

The present Medi-Cal crisis will find some kind of resolution. But a permanent solution to the underlying problems is unlikely. The basic issues will be around to plague government-financed health care plans for a very long time to come. One fundamental issue, and sure to be a recurrent one, is whether government programs are to continue to be patient-oriented or will they become bureaucrat-oriented. It already seems all too obvious that if the needs of the patient are to remain the central focus, there must be a strong advocate of these needs. Medicine can and should be this advocate. It alone has the technical knowledge of what is needed. To fulfill this role and responsibility, it will be necessary for the profession to develop those social, economic and political skills which will make the fragile and intangible strengths of medicine powerful enough to hold their own with the firm and very tangible strengths of government in the decisive arena of public opinion, where the public issues of both medicine and government are ultimately resolved.

Are there not some important lessons to be learned from this Medi-Cal crisis?

[3]A role for medicine in a new era of health care—Fourth Progress Report of the California Medical Association Committee on the Role of Medicine in Society. Calif Med 108:311-315, 388-395, April & May, 1968

Myotonia—A Different Point of View

THE INTERESTING TOPIC of myotonia has been presented in a Specialty Conference by members of the Department of Neurology at the University of California, Davis, published elsewhere in this issue. This editorial will present another classification of this group of disorders with speculations concerning pathogenesis.

The electrophysiological basis of myotonia is a repetitive, decrescendo and decelerating discharge of muscle fibers following voluntary contraction or stimulation by the motor nerve, percussion, or an electrode. Clinically it is a prolonged muscle contraction lasting several seconds or so. Myotonia is only a symptom or physical sign. Rather than classify "the myotonias," it is preferable to list the diseases in which myotonia is found:

1. Clinical myotonia
   a. myotonia atrophica ("myotonia dystrophica")
   b. myotonia congenita

c. paramyotonia - adynamia complex — includes paramyotonia congenita and adynamia episodica hereditaria ("potassium-provoked periodic paralysis" or "hyperkalemic periodic paralysis, idiopathic")
d. hypokalemic periodic paralysis, idiopathic
e. chondrodystrophic myotonia[1]

2. Electromyographic myotonia only — occasional cases
a. denervation[2,3]
b. acid maltase deficiency (Pompe's disease)[4]
c. diazacholesterol[5] or 2,4 - dichlorphenoxyacetate (2,4-D)[6,7] intoxication
d. polymyositis/dermatomyositis

Myotonia congenita is the disease presenting the most prominent and generalized form of myotonia. The initial muscle power may be slightly weak, but after the patient takes a few "warming-up" movements the strength becomes normal or better. These patients do not have attacks of episodic flaccid weakness spontaneously nor is weakness provoked by up to 10 gm of KCl orally.[8]

Paramyotonia congenita has lesser generalized myotonia, which is often evident from infancy (a cold washcloth can bring out myotonia of face and eyelids of the baby). Myotonia in all myotonic diseases is worsened by cold. Cold-provoked episodic flaccid weakness is more characteristic of paramyotonia. There was uncertainty initially about the relation between paramyotonia congenita and adynamia episodica hereditaria, but subsequently paramyotonia patients were shown to have potassium-provoked weakness,[8,9] and myotonia, sometimes in the eyelids only, was found in adynamia patients.[10] It seems to this reviewer that paramyotonia and adynamia represent two extremes of one disorder, the former having more myotonia and less episodic weakness than the latter. To test for potassium-provoked weakness, we give 5, 7.5, and 10 gm oral KCl (68, 101, and 135 mEq) on successive days until a response is obtained; the electrocardiogram is monitored during the test. Since the serum potassium is often not above the normal range during a spontaneous attack of weakness,[10] we prefer to call the disease "potassium-provoked" rather than "hyperkalemic" periodic paralysis. At one time, it was thought that eyelid myotonia could be used to distinguish adynamia from hypokalemic periodic paralysis. Subsequently some cases of clearly documented hypokalemic periodic paralysis were shown to have clinical eyelid myotonia, indicating that this is not a reliable differentiating sign.[11] Myotonia is seen in only occasional cases of hypokalemic periodic paralysis and only in the eyelids.

Electromyographic (EMG) myotonia is seen in several disorders as noted above. The term "myotonia acquisita" has been applied to them. It is a misleading term, its Greco-latinism suggesting a disease rather than simply the denotation of an acquired physical sign. I prefer it be dropped, and for another reason. The myotonia of myotonia atrophica, myotonia congenita and both types of periodic paralysis can also be "acquired" or at least noticed in childhood, or even young adulthood in the first.

There are several clinical phenomena of prolonged muscle contraction which resemble myotonia and must be differentiated from it:

1. Painful contracture after repetitive exercise, no rise of blood lactate—seen in abnormalities of glycogen metabolism, *viz.* phosphorylase deficiency (contracture electrically silent)[12] and phosphofructokinase deficiency (contracture not studied electrically)[13,14]

2. Electrically silent contracture (no mention of pain) after single contraction, normal rise of blood lactate, a congenital familial disease[15,16]

3. Electrically silent painless contracture after strong exercise, normal rise of blood lactate—one report of decreased ability of sarcoplasmic reticulum to accumulate calcium ions[17]

4. Electrically silent delayed relaxation of tendon reflex in myxoedema—caused by a defect of myofiber, probably of contractile mechanisms rather than of cell membrane[16]

5. Massive rigidity associated with malignant hyperthermia during and following general anesthesia—possibly a myofiber defect; one report of impaired calcium uptake by sarcoplasmic reticulum[18]

6. Syndrome of continuous muscle activity—caused by spontaneous discharge of the terminal portions of the lower motor neuron axon; this appears clinically as myokymia, and on EMG as trains of continuous motor unit activity; patients also have hyperhydrosis and elevated basal metabolic rate but normal thyroid function;[2,19,21] they usually do not have true myotonia; are responsive to diphenylhydantoin, carbamazapine, and acetazolamide

7. Cramps, consisting of high frequency trains of discharges of motor units—occur occasionally in normal muscle and more often in diseases of denervation

8. Tetany, in hypocalcemia – attributed to hyperexcitable peripheral nerve fibers[16]

9. Tetanus, from bacterial exotoxin—attributed to suppression of inhibitory synaptic action in the spinal cord[22]

10. Stiff-man syndrome – spontaneous prolonged contractions of central origin[23,24]

11. Spasms from black widow spider bite—site of action unknown[16]

12. Dystonia – spontaneous slow tonic contractions of cerebral origin, with "diseases of basal ganglia," e.g. dystonia musculorum deformans

13. Rigidity – continuous muscle activity of cerebral origin, with "diseases of basal ganglia," e.g. parkinsonism

14. Spasticity – spontaneous prolonged contractions and "stiffness" of central origin, with diseases of the corticospinal tracts.

Myotonia atrophica (or myotonic atrophy) is the most prevalent disease manifesting myotonia, and, in fact, is one of the most prevalent neuromuscular disorders. The term "myotonia atrophica," actually one of the original names of the disease, is preferred as a more literal description of the disease than the currently nearly universally used term "dystrophica myotonica" (or "myotonic dystrophy") of which the word "dystrophy" implies an hereditary disorder of the myofiber which is not secondary to neural involvement.

Myotonia atrophica is a slowly progressive multisystem disease, which includes involvement of the neuromuscular system, ocular lens, scalp hair follicles, and testes. One apparently unique metabolic abnormality has been identified, a short half-life of serum IgG due to hypercatabolism (without complex cryogels),[25] which is the basis of the low serum IgG. There is also an unusual hyperinsulinism without concomitant hypoglycemia.[26,27] The relation of the metabolic abnormalities to the various organ involvements is unknown. We will concern ourselves with the pathogenesis of the muscle weakness, atrophy and myotonia of this disease.

I propose that the muscle involvement in myotonia atrophica is secondary to chronic lower motor neuron (LMN) involvement and thus the disease is a form of neuropathy (used simply to designate a disease of all or part of the LMN) and not a myopathy. Normally the LMN exerts a number of influences on the several hundred muscle fibers (myofibers) it innervates. These LMN-to-myofiber influences can be thought of as "factors" which, for purposes of discussion, are considered to be single and separate.[28] The proposed factors each might be chemically different or related to different patterns or amounts of release of a fewer number of substances. The excitatory factor is acetylcholine. The nature of the postulated trophic factor(s), which maintains myofiber health, diameter, and distinct histochemical type, is unknown. (Perhaps a separate trophic-type factor is responsible for maintaining the histochemical type.) The inhibitory "factor" is postulated to be that influence which keeps an innervated myofiber from discharging spontaneously, that is, from generating fibrillation potentials, as is characteristic of denervated myofibers; its nature is unknown. These factors or their metabolic support system probably are manufactured in a LMN soma and travel in the tide of axoplasmic flow down to its several hundred axon endings. It is proposed that in different diseases the LMN can react with different partial abnormalities, that is, with quantitative or qualitative abnormalities of axoplasmic flow, or both.

Evaluations of the findings in myotonia atrophica in support of this proposed pathogenesis are as follows. The exclusive early muscle lesion is myofiber atrophy without necrosis or phagocytosis.[29-31] In most instances it preferentially affects type I muscle fibers (low in myofibrillar ATPase and phosphorylase high in succinate dehydrogenase, and typed by the first reaction) but in some patients both fiber types are atrophic.[29-31] This atrophy more closely resembles atrophy due to loss of nerve supply than the changes of Duchenne pseudohypertrophic muscular dystrophy (postulated by us to be due to a blood vessel malfunction),[32,33] limb-girdle muscular dystrophy, facioscapulohumeral muscular dystrophy, or oculopharyngeal muscular dystrophy.[34] In more advanced myotonia atrophica, the muscle shows very atrophic fibers, sometimes in groups, clumps of pyknotic nuclei, infrequent necrotic fibers, some hypertrophied fibers, and sometimes slight endomysial connective tissue increase in the more severely affected regions, thus closely resembling what is seen in mid to later stages of neurogenic atrophy.[29-31] Even the multiple internal nuclei of myofibers seen in all stages of the disease conceivably are compatible with a form of neurogenic pathogenesis since they too occur, though not so abundantly, in ordinary chronic denervation. Sarcoplasmic masses, which are usually peripheral

with ring myofibrils just central to them,[29,35] are sometimes seen in myofibers of more severely involved muscle. They too are compatible with the proposed long-standing mild reduction of neural trophic factor, allowing some myofibers to undergo a sort of peripheral degeneration to form the sarcoplasmic masses and, it is proposed, some peripheral myofibrils to break and be pushed by repeated contractions to a ring position—because such peripheral degeneration of milder degree is sometimes seen by electronmicroscopy in experimentally denervated myofibers.[31] Ring myofibrils, as well as snake-coil myofibrils, which seem to be formed in a somewhat similar way, can be found in experimentally denervated muscle.[31,36]

Like chronic neurogenic atrophy, the "muscle enzymes" (SGOT, SGPT, LDH, CPK, and aldolase) are not significantly elevated in myotonia atrophica except for occasional mild increase of CPK,[31] contrasting with what is seen in active myopathy. In myotonia atrophica there are prominent abnormalities of motor nerve endings shown with methylene blue staining.[37,38]

The EMG pattern shows motor unit action potentials of short duration and small amplitude, and units firing more abundantly for a given amount of work. This pattern is usually erroneously called, without further qualification, "myopathic" because it is typically seen in Duchenne muscular dystrophy and certain other myopathies. Preferably it should be given a descriptive, nondiagnostic name, such as a "SSAP" (short, small, abundant potentials) pattern. In Duchenne muscular dystrophy and certain other myopathies it is attributed to loss of some myofibers from all motor units (a motor unit is one LMN and the several hundred myofibers innervated by it) leaving a normal total number of units but each with numerically reduced myofiber content. Such a reduced unit is less than normally efficient and therefore more units must fire to achieve a given amount of work. But it is logical that any disease affecting neuromuscular transmission of some but not all of the myofibers within each motor unit, or affecting only some of the prejunctional distal axonal twigs of each motoneuron "tree," theoretically ought to also give a SSAP pattern. Just as when the flow of sap in a tree diminishes in autumn and some of the leaves fall before others (the most distal leaves fall first in sugar maples), it is proposed that when the LMN soma does not adequately nourish some of the axon tips in myotonia atrophica, corresponding myofibers within each motor unit atrophy and eventually fail to respond to motor nerve firing (perhaps because of failure of axon tips to conduct) and thus cause an SSAP pattern. Another mechanism possibly contributing to the SSAP pattern in some patients is the selective atrophy of their type I myofibers.[39]

Clinical myotonia is a repetitive discharge of many myofibers. From an individual myofiber the individual EMG wave forms of myotonia usually are indistinguishable from fibrillation potentials or positive sharp waves, both characteristic of a denervated myofiber. The myotonia waves also look like denervated fiber activity with intracellular microelectrodes.[40] A similar repetitive discharge was recorded from individual myofibers of chick embryos growing in tissue culture without nerve.[41] The myotonic potentials are generated from the abnormally labile myofiber membrane, but normally the nerve controls the stability of that membrane. We propose that a decrease of inhibitory influence ("inhibitory factor") from the LMN to muscle allows manifestation of myotonia.[28] "Pseudomyotonia" is the EMG term applied to a myotonia-like train of repetitive potentials that end abruptly rather than by decrescendo. The individual potentials are like the initial ones of myotonia. The distinction between pseudomyotonia and myotonia is probably not significant; both are likely to be caused by a very similar or the same defect of the myofiber membrane. We postulate that both are due to defective neural inhibitory factor. Pseudomyotonia, and sometimes true myotonia, can be seen in denervation. It is not known whether the myotonia in acid maltase deficiency is related to the known LMN soma abnormality[42] or myofiber abnormality, or both, of that disease. The pathogenesis of experimental myotonia induced by diazacholesterol and 2,4-D is not yet known. Polymyositis and dermatomyositis can have involvement of nerve endings histologically.[37]

Usually the motor nerve conduction time is normal in myotonia atrophica, which is compatible with preserved motor axon conduction function in the presence of decrease in only some of the neuronal factors to muscle.

The cerebralspinal fluid sometimes shows slightly or moderately elevated protein.[31,43] In many cases there is a mild aberration of thinking and sometimes frank retardation or dementia.

More advanced cases may have dilated cerebral ventricles.[44] These all point to some type of central nervous system involvement in myotonia atrophica. The motor nerves and motoneuron somas in the anterior horn of the spinal cord have not been considered to be morphologically abnormal, although newer techniques of histochemistry and electronmicroscopy have not been applied. Nevertheless, the motoneurons could be functionally abnormal while retaining a normal morphologic appearance.

The neuromuscular manifestations of myotonia atrophica are compatible with a chronic, neurogenic pathogenesis, which we prefer rather than a myogenic one. We propose that the disease is basically a chronic, partial defect of neuronal influence on muscle, mainly of neuronal trophic factor and inhibitory factor, with lesser defect of excitatory factor function. The defect is associated with abnormalities in distal portions of some axonal tips of each motor unit, which in turn may stem from abnormality of the motor neuron soma; this would be a mechanism similar to diminished axoplasmic flow induced by the neurotoxin acrylamide.[45] Perhaps the defect usually involves type I motoneurons more severely, though it could also be related to a greater susceptibility of type I myofibers to the abnormality. There is no basis for suggesting whether such a proposed LMN involvement is due to an inherited defect of LMN metabolism or the LMN metabolism is affected adversely by abnormality of another tissue which produces a detrimental influence or fails to provide a necessary influence required by the LMN. The implication of this neurogenic hypothesis for the neuromuscular involvement of myotonia atrophica is that the LMN and influences upon it must be studied rather than the muscle, which is viewed as a passive victim of effete neurons. It is concluded that myotonia atrophica is mainly a form of neuropathy, not a myopathy or muscular dystrophy. Whether there is a minor element of myopathy too is perhaps a possibility, but according to this hypothesis it is not the major pathogenesis.

If myotonia atrophica might be due to abnormality of neural influence on muscle, we must consider that myotonia congenita also may be, but caused by an abnormality involving a preferential loss of neural inhibitory factor (to release myotonia) rather than trophic factor. There is no myofiber atrophy early in the disease, though later there may be atrophy of scattered fibers. Finally, the possibility of a neuropathic element, perhaps as a minor aspect of the pathogenesis, must be raised in potassium-provoked and hypokalemic forms of periodic paralysis, both of which can have some myotonia. The hypokalemic periodic paralysis typically has myofiber atrophy, roughly proportional to the duration and severity of disease.[46]

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Diagnosis and Treatment of Pemphigus

THE REVIEW ON "Recent Advances in the Diagnosis and Treatment of Pemphigus" by Newcomer and Landau printed in this issue emphasizes the important effects of the discovery of circulating antibodies in pemphigus and in bullous pemphigoid. The etiologic concepts of these diseases as well as diagnosis and treatment have been affected.

With regard to etiology, the authors cite the available evidence indicating that the antibodies might be the cause of the disease in pemphigus and bullous pemphigoid. Although many factors speak in favor of this concept, the ultimate proof for it—namely, the passive transfer of the disease by means of its antibodies—may never be attained. Still, it can be said that lesions analogous to those of pemphigus vulgaris have been reproduced in animals by the experimental production of intercellular antibodies in such animals. Also, in addition to the evidence cited by the authors, it would seem that the favorable results obtained with methotrexate in the treatment of both pemphigus and bullous pemphigoid favor the concept of autoimmunity as a causative factor. In addition, the occasional coexistence of pemphigus with other immunological disorders, such as lupus erythematosus, rheumatoid arthritis and myasthenia gravis, indicates pemphigus too may be an autoimmune disorder, even though in most instances the additional immunologic disorder coexisting with pemphigus is silent and evident only by laboratory tests.

The diagnostic value of the demonstration of "antiepithelial" antibodies in pemphigus and of "basement zone" antibodies in bullous pemphigoid is considerable since these antibodies are specific for pemphigus and bullous pemphigoid, respectively. With adequate controls it is possible to avoid false positive results such as were obtained by the authors when fortuitously they used as substrate the esophagus of a rhesus monkey possessing blood-group-B substance. This resulted in fluorescence when serum from patients having anti-B isohemagglutinins in their blood was tested.

There is, however, a drawback in the antibody determination method for diagnositic purposes in that it may give negative results in the early stage of pemphigus or bullous pemphigoid when only a few lesions are present. Possibly, with improvement of the technique and the substitution of peroxidase-labeled antibodies for fluorescein-labeled antibodies, the incidence of false negative results can be reduced in the future. However, as was pointed out by the authors, it actually is not necessary to use indirect immunofluorescent testing for routine diagnostic purposes, since in most instances histologic examination is adequate for diagnostic clarification. Also, histologic examination enables one to dif-